Appl. No. : **10/036,342**
Filed : **December 26, 2001**

SUMMARY OF THE INTERVIEW

Applicants thank Examiner Kolker and Supervisor Turner for the telephone interview on September 21, 2005 with Applicants' representative Marc Morley.

Exhibits and/or Demonstrations

None.

Identification of Claims Discussed

Claims 22-30 and 32-34 were discussed.

Identification of Art Discussed

U.S. Publication No. 2003/0100051 (Ruben et al.) was discussed.

Proposed Amendments

None.

Principal Arguments and Other Matters

The interview participants discussed the issues and rejections set forth in the July 29, 2005 Office Action, including the IDS issue, the oath/declaration issue, the utility rejection, the § 112 rejections, and the § 102 rejection.

Results of Interview

No agreement was reached with respect to claim language.

Appl. No. : **10/036,342**
Filed : **December 26, 2001**

REMARKS

The claims have been amended as set forth above. Upon entry of the above-described amendments, Claims 22-30 and 32-34 are pending. Claims 22-27 and 30 have been amended to remove reference to the "extracellular domain." Support for this amendment is found, for example, in Figure 26. Thus, no new matter is added by the amendments and the claims are fully supported by the specification as originally filed.

Applicants respond below to the specific rejections raised by the Examiner in the Office Action mailed July 29, 2005. For the reasons set forth below, Applicants respectfully traverse.

Information Disclosure Statement

Applicants previously provided the Patent Office with an Information Disclosure Statement (IDS) that included BLAST results. In the Office Action, the Examiner indicates that the IDS has been considered, but that the BLAST results cannot be considered. During the Interview the Examiner clarified that the submitted IDS had been considered, but that the entry for the BLAST results was crossed out on the Form 1449 because BLAST results were not typical "publications" that could be searched or indexed. As such, the BLAST results were considered by the Patent Office, but would not be listed on the face of any patent that issues.

Oath/Declaration

The Examiner states that the oath or declaration is defective, and states that a new oath or declaration in compliance with 37 C.F.R. § 1.67(a). The Examiner argues that the original oath or declaration is defective because of non-initialed and/or non-dated alterations by Zhang and Eaton.

As discussed during the September 21st interview, Zhang and Eaton were previously deleted as inventors. Therefore, a new declaration from Zhang and Eaton is not required and the rejection is moot.

Rejection under 35 U.S.C. §101 - Utility

The Examiner maintained the rejection of Claims 22-30 and 32-34 under 35 U.S.C. § 101 because allegedly the claims lack utility. The Examiner acknowledges that the claims were not rejected for lack of a specific or credible utility, but only for lacking a substantial utility. In the

Office Action, the Examiner acknowledges that the proliferation of kidney mesangial cells is useful. However, the Examiner argues that the threshold used to determine a "positive" in the mesangial cell assay of Example 41 would not be considered reasonable by one of skill in the art, relying upon the post-filing publication by Rovin et al. The Examiner points to one passage in Rovin et al. where a particular data point reportedly was not statistically significant. Thus, the Examiner concludes in view of Rovin et al. that "the specification does not disclose the variability in the sample, so a skilled artisan would not reasonably conclude that PRO4380 induces mesangial cell proliferation."

Rovin et al. is Irrelevant to the Utility of the Claimed Subject matter

Applicants respectfully disagree with the instant utility rejection and with the utility standard that is being applied by the Office. Applicants have satisfied the utility requirement when the correct standard is applied. Applicants respectfully remind the Patent Office that "[a]ny reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a 'substantial' utility." (M.P.E.P. 2107.01). An Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. § 101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope." Here, there is no reason to doubt or question the utility of PRO4380 which tested positive in the mesangial cell proliferation assay.

Example 41 of the specification describes a kidney mesangial cell proliferation assay. PRO4380 tested positive in the assay. Such activity satisfies the utility requirement under § 101. As discussed during the interview, the article by Rovin et al. is irrelevant to the utility of the instant claims. The passage relied upon by the Examiner stated that for the tested compound ciglitazone (at a concentration of 5 μmol/L), the results were not statistically significant. Thus, Rovin et al. merely demonstrates that for the particular tested compound, ciglitazone, it is not possible to tell if the compound caused an outcome that was different from the outcome seen for the control sample. In other words, the particular data point lacked statistical certainty or significance. As discussed during the interview, the statistical significance of the ciglitazone data point in Rovin et al. is completely irrelevant to Applicants assay as described in Example 41. Here, PRO4380 tested positive in the kidney mesangial cell proliferation assay, and as such, the

utility requirement is satisfied. The fact that Rovin et al. reported a statistically insignificant data point has no bearing on Applicants' assay results.

A Substance that Induces Mesangial Cell Proliferation is Useful

During the telephone interview on September 21st, the Patent Office representatives also asked how a substance that tested positive in the assay of Example 41 might be useful. Applicants submit that the usefulness of such a substance is clear from the specification. Nonetheless, as a further explanation, a substance that induces proliferation of kidney mesangial cells can be biologically or therapeutically useful for a number of reasons. Generally, such a substance can be used to repair damaged tissue and to restore proper kidney function. *See* Example 41 of the specification. Also, in instances where mesangial cell growth is out of balance or contributes to a disease condition, a substance that contributes to proliferation can be inhibited or blocked. *See* specification at page 119, line 4 to page 122, line 8 ("Uses for PRO") and at page 134, line 14 to page 135, line 14 ("Pharmaceutical Compositions of Antibodies"). These uses are explained in more detail below.

Mesangial cells are important components for the proper function and structure of the kidneys. They are fundamental cells that aid in the filtration of blood by the kidneys. Mesangial cells are located among the glomerular capillaries within a renal corpuscle. Glomerular capillaries consist of endothelial cells with large fenestrations, and are therefore very permeable ("leaky") for most solutes in blood plasma. Mesangial cells aid in the regulation of glomerular filtration. They are also major contributors to the important extracellular matrix in the glomeruli. In various renal diseases, mesangial cells and other cells are damaged, which leads the loss of renal function.

As mentioned above, a substance that induces mesangial cell proliferation can be used in tissue repair and to restore mesangial cell function. As mentioned above, the result of a variety of kidney diseases or kidney injuries is a deficiency or destruction of kidney mesangial cells, which leads to decreased kidney function. As set forth in Example 41, a molecule that induces proliferation of mesangial cells can be useful for the treatment of various kidney/renal disorders, for example, those associated with decreased mesangial cell functions, such as, Berger disease or other nephropathies associated with Schönlein-Henoch purpura, celiac disease, dermatitis herpetiformis or Crohn disease. A substance that induces proliferation of mesangial cells can be

used to regenerate mesangial cells and to repair or restore damaged tissue, thereby restoring proper kidney function. As discussed with the Examiner, a number of scientific literature papers describe efforts to generate mesangial cells in order to repair damaged kidney tissue in the context of glomerular repair or remodeling. *See for example*, Hugo et al., "Extraglomerular Origin of the Mesangial Cell after Injury," *J. Clin. Invest.*, 100:786-794, 1997; Ito et al., "Bone Marrow is a Reservoir of Repopulating Mesangial Cells during Glomerular Remodeling," *J. Am. Soc. Nephrol.*, 12:2625-2635, 2001; and Zhang et al., "Participation of endothelial cells and transformed mesangial cells in remodeling of glomerular capillary loops in Thy-1 nephritis," *Pathol. Int.*, 51:227-239, 2001.

Second, a substance that induces proliferation is useful because it can be blocked or inhibited. In some disease conditions improperly regulated mesangial cells can contribute to the disease pathology. In such cases, the instant PRO molecule can be blocked or inhibited in order to decrease the proliferation of mesangial cells. The blocking or inhibition can be done, for example, at the nucleic acid level or at the polypeptide level. The specification in various locations describes how to block the nucleic acid that encodes the PRO molecule and also describes anti-PRO antibodies. *See* page 119, line 4 to page 122, line 8 ("Uses for PRO") and page 134, line 14 to page 135, line 14 ("Pharmaceutical Compositions of Antibodies").

The preceding paragraphs describe, consistent with the disclosure in the specification, exemplary uses for the polypeptides that are able to induce mesangial cell proliferation. Applicants note that "Courts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an 'immediate benefit to the public' and thus satisfies the utility requirement." M.P.E.P. § 2107. As the Court of Customs and Patent Appeals held in *Nelson v. Bowler*:

> Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility.

Here, Example 41 demonstrates that PRO4380 has activity in that it is capable of inducing kidney mesangial cell proliferation. The Federal courts have consistently reversed rejections by the Office asserting a lack of utility for inventions claiming a pharmacological or

therapeutic utility where an applicant has provided evidence that reasonably supports such a utility. *See* M.P.E.P. § 2107.03. This is not one of the cases where the asserted utility is vague and generalized. *See id.* In view of the above discussion, Applicants respectfully request reconsideration and withdrawal of the instant utility rejection under 35 U.S.C. § 101.

Rejections under 35 U.S.C. §112, first paragraph – Enablement

The Examiner has maintained the rejection of Claims 22-30 and 32-34 under 35 U.S.C. § 112, first paragraph, for lacking enablement. According to the Examiner, because the claimed invention is not supported by either a substantial asserted utility or a well established utility, one of skill in the art would not know how to use the invention.

Applicants submit that in the above discussion of the rejection under 35 U.S.C. § 101, Applicants have established a substantial, specific, and credible utility for the claimed polypeptides. Specifically, the claimed polypeptides have utility in inducing mesangial cell proliferation.

The Examiner further rejects the variant claims arguing that "[e]ven if enablement were found for PRO4380, enablement would not be commensurate in scope with claims [22-26] because the specification does not reasonably provide enablement for polypeptides 80%, 85%, 90%, 95%, or 99% identical to SEQ ID NO:57 which have the ability to induce mesangial cell proliferation." The Examiner supports this rejection by arguing that SEQ ID NO:57 is deemed to be unable to induce mesangial cell proliferation for the reasons specified in the utility rejection in connection with Rovin et al.

For the reasons discussed above, the Examiner's argument based upon Rovin et al. is irrelevant and Example 41 in the specification shows that SEQ ID NO:57 induces mesangial cell proliferation. Thus, the variant claims are enabled.

Therefore, Applicants request that the Examiner reconsider and withdraw the enablement rejection under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. §112, first paragraph – Written Description

The Examiner continues to reject Claims 22-26 and 33-34 arguing that those claims contain subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner argues that the inclusion of the limitation that the polypeptide variants have the ability to induce mesangial cell proliferation fails to meet the written description requirement.

Respectfully, the Examiner has given no weight to the claim limitation, "wherein said isolated polypeptide has the ability to induce mesangial cell proliferation." Presumably, this is because the Examiner believes that SEQ ID NO:57 is unable to induce mesangial cell proliferation for the reasons specified in the utility rejection.

In view of Applicants' arguments above regarding the validity of the mesangial cell assay in Example 41 and the irrelevance of Rovin et al., reconsideration and withdrawal of this rejection is requested.

New Rejection under 35 U.S.C. §112, first paragraph – New Matter

The Examiner rejects Claims 22-30 and 32-34 under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. According to the Examiner, the previous claim amendment to recite "wherein the extracellular domain is amino acids 293-507," constitutes new matter because the there is no disclosure of that region being extracellular.

As shown above, Claims 22-27 and 30 have been amended to remove reference to the "extracellular domain." Therefore, this rejection is moot.

Rejection under 35 U.S.C. §102 – Anticipation

The Examiner withdrew the previous rejection under 35 U.S.C. § 102(a) in view of Applicants' previously filed response and declaration. The Examiner now rejects Claims 22-27, 29-3 and 33-34 as anticipated under 35 U.S.C. § 102(e) by U.S. Patent Publication No. 2003/0100051 (Ruben et al.), which was published on May 29, 2003. The Examiner argues that the published application has an effective publication date under § 102(e) of May 12, 1998 or May 18, 1998 based upon 13 provisional applications filed on those dates. The Examiner states that the reference teaches an anticipating amino acid sequences that is 97% to 100% identical to the claimed polypeptides. Applicants respectfully traverse.

Appl. No. : 10/036,342
Filed : December 26, 2001

As an initial matter, Applicants note that Ruben et al. is a continuation-in-part (CIP) of U.S. Application No. 09/892,877 filed on June 28, 2001, which is a continuation of U.S. Application No. 09/437,658 filed on November 10, 1999, which is a CIP of PCT Application No. PCT/US99/09847 filed on May 6, 1999, which claimed priority to 13 provisional applications filed on May 12, 1998 or May 18, 1998. In view of this, the Examiner argues that the earliest effective publication date under § 102(e) of Ruben et al. is May 12, 1998. Applicants disagree. Ruben et al. claimed the benefit of an international (PCT) application that was filed before November 29, 2000. Ruben et al. cannot be given the filing date of the PCT application, or the preceding provisional applications, under § 102(e) for prior art purposes. *See* M.P.E.P. § 706.02(f). Therefore, the prior art date of Ruben et al. under § 102(e) is November 10, 1999.

Attached herewith is the Declaration of Audrey Goddard, Paul J. Godowski, Austin L. Gurney, James Pan, Colin K. Watanabe and William I. Wood under 37 C.F.R. §1.131 (referred to hereafter as "the Declaration of Goddard et al."), which establishes that the presently claimed invention antedates the publication date of Ruben et al. The Declaration is submitted with this response in seven (7) pages with the signature of each inventor on a separate page. Applicants note that inventor Austin Gurney ("Gurney") signed the Declaration on the line provided for inventor James Pan ("Pan"). Thus, there are two pages with signatures on the line for James Pan, one signature is by Gurney and the other signature is by Pan.

The Declaration of Goddard et al. establishes that the presently claimed subject matter was conceived of and reduced to practice prior to the § 102(e) prior art date of Ruben et al., November 10, 1999. Thus, Applicants respectfully submit that the cited reference is not available as prior art, and request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

As set forth in 37 C.F.R. § 1.131, a patent applicant "may submit an appropriate oath or declaration to establish invention of the subject matter of the rejected claim prior to the effective date of the reference or activity on which the rejection is based." *See also*, M.P.E.P. § 715. "The affidavit or declaration must state FACTS and produce such documentary evidence and exhibits in support thereof as are available to show conception and completion of the invention in this country ... at least conception being at a date prior to the effective date of the reference." *See* M.P.E.P. § 715.07 (emphasis in original). The showing of facts must be sufficient to show

"conception of the invention prior to the effective date of the reference coupled with due diligence from prior to the reference date to a subsequent (actual) reduction to practice." *See id.*

As mentioned above, Ruben et al. has a prior art date under § 102(e) of November 10, 1999. Ruben et al. is cited as a § 102(e) reference because it allegedly discloses an amino acid sequence that is 97% to 100% identical to the claimed polypeptides. However, as set forth below, Applicants were in possession of SEQ ID NO: 57 prior to the § 102(e) date of Ruben et al.

The Declaration and attached Exhibit A demonstrate that the claimed subject matter, particularly a polypeptide having the sequence of SEQ ID NO: 57, was conceived by Applicants prior to November 10, 1999. Furthermore, as evidenced by the Declaration and Exhibit B, Applicants reduced the subject matter of the claims to practice prior to the § 102(e) date of Ruben et al., by performing assays to confirm the function of the polypeptide. Therefore, Applicants possessed the claimed subject matter prior to the publication date of the cited reference.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 102.

Conclusion

The present application is believed to be in condition for allowance, and an early action to that effect is respectfully solicited. Applicants invite the Examiner to call the undersigned if any issues may be resolved through a telephonic conversation.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 10/28/05

By: _____

Marc T. Morley
Registration No. 52,051
Attorney of Record
Customer No. 30,313
(619) 235-8550

2021535; 102505